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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	NOV 21	CAS patent coverage to include exemplified prophetic substances identified in English-, French-, German-, and Japanese-language basic patents from 2004-present
NEWS 3	NOV 26	MARPAT enhanced with FSORT command
NEWS 4	NOV 26	CHEMSAFE now available on STN Easy
NEWS 5	NOV 26	Two new SET commands increase convenience of STN searching
NEWS 6	DEC 01	ChemPort single article sales feature unavailable
NEWS 7	DEC 12	GBFULL now offers single source for full-text coverage of complete UK patent families
NEWS 8	DEC 17	Fifty-one pharmaceutical ingredients added to PS
NEWS 9	JAN 06	The retention policy for unread STNmail messages will change in 2009 for STN-Columbus and STN-Tokyo
NEWS 10	JAN 07	WPIDS, WPINDEX, and WPIX enhanced Japanese Patent Classification Data
NEWS 11	FEB 02	Simultaneous left and right truncation (SLART) added for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
NEWS 12	FEB 02	GENBANK enhanced with SET PLURALS and SET SPELLING
NEWS 13	FEB 06	Patent sequence location (PSL) data added to USGENE
NEWS 14	FEB 10	COMPENDEX reloaded and enhanced
NEWS 15	FEB 11	WTEXTILES reloaded and enhanced
NEWS 16	FEB 19	New patent-examiner citations in 300,000 CA/CAplus patent records provide insights into related prior art
NEWS 17	FEB 19	Increase the precision of your patent queries -- use terms from the IPC Thesaurus, Version 2009.01
NEWS 18	FEB 23	Several formats for image display and print options discontinued in USPATFULL and USPAT2
NEWS 19	FEB 23	MEDLINE now offers more precise author group fields and 2009 MeSH terms
NEWS 20	FEB 23	TOXCENTER updates mirror those of MEDLINE - more precise author group fields and 2009 MeSH terms
NEWS 21	FEB 23	Three million new patent records blast AEROSPACE into STN patent clusters
NEWS 22	FEB 25	USGENE enhanced with patent family and legal status display data from INPADOCDB
NEWS 23	MAR 06	INPADOCDB and INPAFAMDB enhanced with new display formats

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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 NEWS IPC8     For general information regarding STN implementation of IPC 8

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.22       0.22

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DICTIONARY FILE UPDATES:   6 MAR 2009  HIGHEST RN 1116745-20-0

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=>
Uploading C:\Program Files\STNEXP\Queries\10599918 protection of I.str
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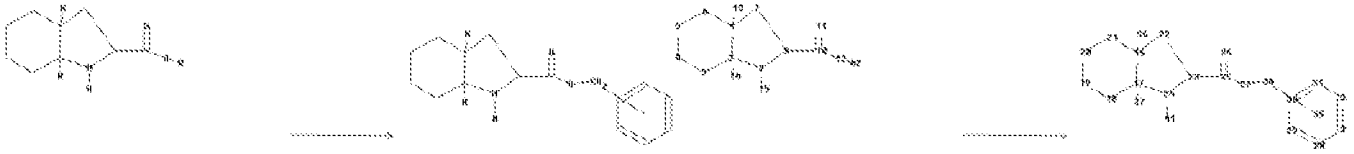

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10  11  12  13  14  15  25  26  27  34  36  37  41  42
ring nodes :
1  2  3  4  5  6  7  8  9  16  17  18  19  20  21  22  23  24  28  29  30  31  32
```

```
33
chain bonds :
1-13  2-14  8-10  9-15  10-11  10-12  12-42  16-36  17-37  23-25  24-41  25-26  25-
27
27-34
ring bonds :
1-2  1-6  1-7  2-3  2-9  3-4  4-5  5-6  7-8  8-9  16-17  16-21  16-22  17-18  17-24
18-19  19-20  20-21  22-23  23-24  28-29  28-33  29-30  30-31  31-32  32-33
exact/norm bonds :
2-9  8-9  17-24  23-24  25-26  25-27
exact bonds :
1-2  1-6  1-7  1-13  2-3  2-14  3-4  4-5  5-6  7-8  8-10  9-15  12-42  16-17  16-21
16-22  16-36  17-18  17-37  18-19  19-20  20-21  22-23  23-25  24-41  27-34
normalized bonds :
10-11  10-12  28-29  28-33  29-30  30-31  31-32  32-33
isolated ring systems :
containing 1 : 16 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:CLASS
11:CLASS  12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:Atom  17:Atom  18:Atom  19:Atom
20:Atom  21:Atom
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31:Atom
32:Atom  33:Atom  34:CLASS  35:Atom  36:CLASS  37:CLASS  41:CLASS  42:CLASS
fragments assigned product role:
containing 16
fragments assigned reactant/reagent role:
containing 1




L1      STRUCTURE UPLOADED

=> d L1
L1 HAS NO ANSWERS
L1              STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.


=> file casreact
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.48       0.70

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```

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*************************************************************
*                                                           *
*     CASREACT now has more than 16.5 million reactions     *
*                                                           *
*************************************************************
```


This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s L1 SSS full
FULL SEARCH INITIATED 12:55:19 FILE 'CASREACT'
SCREENING COMPLETE -      633 REACTIONS TO VERIFY FROM       82 DOCUMENTS

100.0% DONE     633 VERIFIED      40 HIT RXNS                      22 DOCS
SEARCH TIME: 00.00.02

L2           22 SEA SSS FUL L1 (    40 REACTIONS)

=> d ibib abs fhit 1-
YOU HAVE REQUESTED DATA FROM 22 ANSWERS - CONTINUE? Y/(N):y
```

L2 ANSWER 1 OF 22 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 149:402630 CASREACT Full-text

TITLE: Efficient access to enantiomerically pure cyclic α-amino esters through a lipase-catalyzed kinetic resolution

AUTHOR(S): Alatorre-Santamaria, Sergio; Rodriguez-Mata, Maria; Gotor-Fernandez, Vicente; de Mattos, Marcos Carlos; Sayago, Francisco J.; Jimenez, Ana I.; Cativiela, Carlos; Gotor, Vicente

CORPORATE SOURCE: Departamento de Quimica Organica e Inorganica, Instituto Universitario de Biotecnologia de Asturias, Universidad de Oviedo, Oviedo (Asturias), 33071, Spain

SOURCE: Tetrahedron: Asymmetry (2008), 19(14), 1714-1719
CODEN: TASYE3; ISSN: 0957-4166

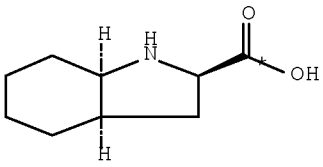
PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

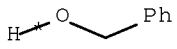
LANGUAGE: English

AB A series of α-amino acid derivs. containing the 2,3-dihydroindole or octahydroindole core have been chemoenzymically synthesized in good overall yields and high enantiomeric purity under mild reaction conditions using lipases for the introduction of chirality. Candida antarctica lipase type A has shown excellent activity and high enantiodiscrimination ability toward the two cyclic amino esters used as substrates. The selectivity of the process proved to be greatly dependent on the alkoxycarbonylating agent. Thus, the enzymic kinetic resolution of Me indoline-2-carboxylate has been successfully achieved using 3-methoxyphenyl allyl carbonate, whereas (2R,3aR,7aR)-benzyl octahydroindole-2-carboxylate required the less reactive diallyl carbonate.

RX(7) OF 32 ...P + U ===> V...

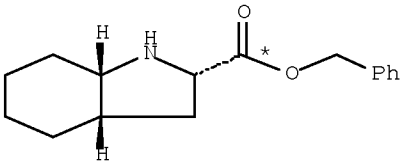


P



U

(7) →



V
YIELD 90%

RX(7) RCT P 80828-13-3, U 100-51-6

STAGE(1)
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe
CON 4 hours, reflux

STAGE(2)
RGT E 144-55-8 NaHCO3
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON room temperature

PRO V 960039-95-6
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:32187 CASREACT Full-text
TITLE: Process for preparation of heterocyclic carboxylic acid esters and heterocyclic amino acid esters
INVENTOR(S): Su, Weike; Xia, Jiansheng; Bian, Gaofeng; Xie, Yuanyuan
PATENT ASSIGNEE(S): Zhejiang University of Technology, Peop. Rep. China; Zhejiang Changming Pharmaceutical Co., Ltd.
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 15pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese

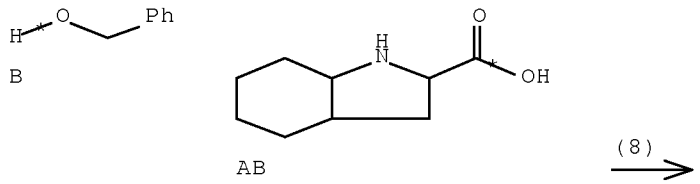
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

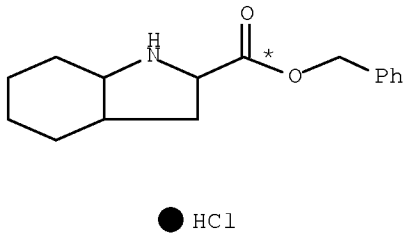
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 101177370	A	20080514	CN 2007-10156706	20071123

PRIORITY APPLN. INFO.: CN 2007-10156706 20071123

AB The title method comprises esterifying alc. with heterocyclic carboxylic acid or heterocyclic amino acid and bis(trichloromethyl) carbonate in the presence of catalyst at 0-100°C for 1-36 h, crystallizing at (-5)-40°C for 1-10 h, and post-treating. The inventive method has the advantages of advanced synthesis route, rational condition, simple and safe process, high yield, low production cost, and low contamination.

RX(8) OF 10 B + AB ===> AG





AG
YIELD 97%

RX(8) RCT B 100-51-6, AB 82717-40-6
RGT D 32315-10-9 (Cl3CO)2CO
PRO AG 82717-97-3
CAT 998-40-3 PBu3
SOL 25551-13-7 Benzene, trimethyl-
CON SUBSTAGE(1) 20 hours, 20 - 30 deg C
SUBSTAGE(2) 30 deg C -> 15 deg C
SUBSTAGE(3) 6 hours, 10 - 15 deg C

L2 ANSWER 3 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 148:471858 CASREACT Full-text
TITLE: Process for industrially viable preparation of esters

of (S,S,S)-octahydroindoline-2-carboxylic acid

INVENTOR(S): Babu, Potluri Ramesh; Hariharakrishnan, Venkata Subramanian; Chowdary, Mulakala Atchuta Ramayya; Kodali, Hariprasad

PATENT ASSIGNEE(S): India

SOURCE: Indian Pat. Appl., 12pp.
CODEN: INXXBQ

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

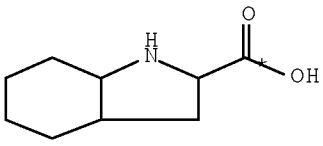
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 2005CH00784	A	20070727	IN 2005-CH784	20050623

PRIORITY APPLN. INFO.: IN 2005-CH784 20050623

OTHER SOURCE(S): MARPAT 148:471858

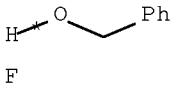
AB The invention relates to a method for the preparation of esters of (S,S,S)-octahydroindoline-2-carboxylic acid ester. (S,S,S)-Octahydroindoline-2-carboxylic acid benzyl ester was prepared by hydrogenation of hexahydroindoline-2-carboxylic acid to give octahydroindoline-2-carboxylic acid, which underwent esterification with benzyl alc. to give the corresponding ester, which under went resolution with chiral agents to give (S,S,S)-octahydroindoline-2-carboxylic acid benzyl ester.

RX(2) OF 3 ...B + F ===> G



● HCl

B



F

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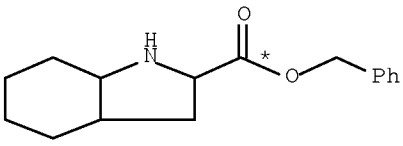


● HCl

G

RX(2) RCT B 110623-68-2, F 100-51-6

STAGE(1)
RGT H 104-15-4 TsOH
SOL 108-88-3 PhMe
CON SUBSTAGE(1) room temperature
SUBSTAGE(3) 25 - 30 deg C

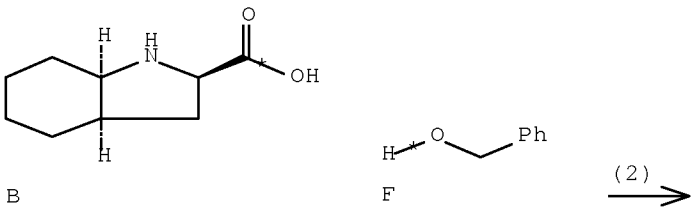
STAGE(2)
SOL 7732-18-5 Water
CON pH 10.5

STAGE(3)
RGT I 7647-01-0 HCl
SOL 67-56-1 MeOH
CON SUBSTAGE(2) 10 - 15 deg C

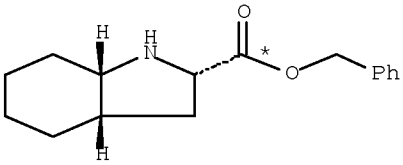
PRO G 82717-97-3

L2 ANSWER 4 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 148:79277 CASREACT Full-text
TITLE: Efficient access to N-protected derivatives of (R,R,R)- and (S,S,S)-octahydroindole-2-carboxylic acid by HPLC resolution
AUTHOR(S): Sayago, Francisco J.; Jimenez, Ana I.; Cativiela, Carlos
CORPORATE SOURCE: Departamento de Quimica Organica, Instituto de Ciencia de Materiales de Aragon, Universidad de Zaragoza-CSIC, Zaragoza, 50009, Spain
SOURCE: Tetrahedron: Asymmetry (2007), 18(19), 2358-2364
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The preparation of the proline analog (2S,3aS,7aS)-octahydroindole-2-carboxylic acid (Oic) and its enantiomer, (2R,3aR,7aR)-Oic, is described. A racemic precursor has been synthesized in good yield and subjected to HPLC resolution on a chiral column. The high efficiency of both the synthetic and chromatog. procedures has allowed the isolation of multigram quantities of each amino acid in enantiomerically pure form and suitably protected for use in peptide synthesis.

RX(2) OF 20 ...B + F ===> G...



B F



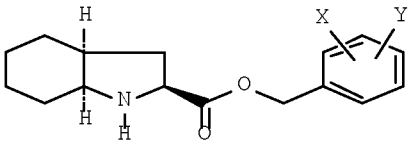
G
YIELD 92%

RX(2) RCT B 80828-13-3, F 100-51-6
RGT H 6192-52-5 p-MeC6H4SO3H.H20
PRO G 960039-95-6
SOL 108-88-3 PhMe
CON 4 hours, reflux
NTE Dean-Stark trap used
REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

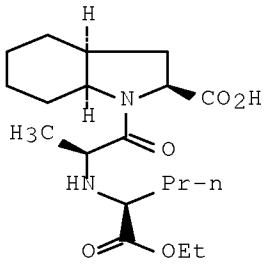
L2 ANSWER 5 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 148:55381 CASREACT Full-text
TITLE: Process for the preparation of perindopril and intermediates thereof
INVENTOR(S): Haider, Akhtar; Megevand, Sophie; Nicollier, Brigitte; Pannatier, Yvan
PATENT ASSIGNEE(S): Sochinaz SA, Switz.
SOURCE: Eur. Pat. Appl., 19pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1864973	A1	20071212	EP 2006-11981	20060609
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRIORITY APPLN. INFO.: EP 2006-11981 20060609
OTHER SOURCE(S): MARPAT 148:55381
GI



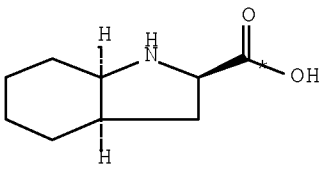
II



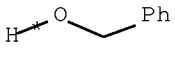
III

AB The invention provides a novel method for the synthesis of (2S,3αS,7αS)-octahydroindole-2-carboxylic acid (I) and its aryl esters II [wherein X, Y = H, halo, alkyl, alkoxyl or nitro group], and the conversion of the p-nitrobenzyl ester of the acid into perindopril or its salts. II were obtained via esterification of racemic octahydroindole-2-carboxylic acid hydrochloride with benzyl alcs. in the presence of aryl sulfonic acids such as p-TsOH, followed by resolution with such as dibenzoyl-(L)-tartaric acid. Alternatively, II could be synthesized directly by esterification of chiral I with benzyl alcs. For example, I was reacted with p-nitrobenzyl alc. in the presence of p-TsOH to afford p-tosylate salt of the corresponding ester in 79% yield, which underwent DCC/HOBt-mediated coupling reaction with N-[(S)-1-(ethoxycarbonyl)butyl]-(S)-alanine in dichloromethane (80% yield). Pd/C-catalyzed hydrogenolysis of the resultant p-nitrobenzyl ester led to perindopril.

RX(2) OF 21 ...B + F ===> G...

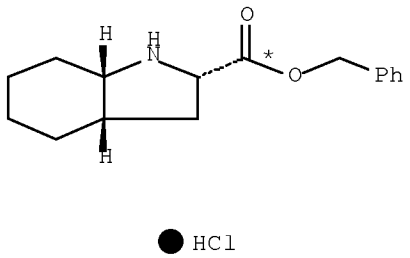


B



F

(2) →



G

RX(2) RCT B 84324-13-0, F 100-51-6
RGT H 104-15-4 TsOH
PRO G 959984-63-5
SOL 108-88-3 PhMe
CON SUBSTAGE(2) 25 - 30 deg C
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 147:541727 CASREACT Full-text
TITLE: Process for the preparation of trandolapril and intermediates thereof
INVENTOR(S): Joshi, Narendra Shriram; Bhirud, Shekhar Bhaskar; Ramam, Buddhavarapu Pattabhi; Bodkhe, Arjun Rajaram
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Limited, India
SOURCE: Indian Pat. Appl., 31pp.
CODEN: INXXBQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 2004MU01060	A	20060728	IN 2004-MU1060	20041007

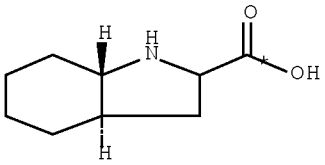
PRIORITY APPLN. INFO.: IN 2004-MU1060 20041007
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

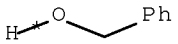
AB The invention relates to a process for the preparation of (2S, 3aR, 7aS)-octahydroindole-2-carboxylic acid (I), and its use for the preparation of trandolapril (II). Trandolapril is an angiotensin-converting enzyme (ACE) inhibitor and is used for the treatment of hypertension. The process of the invention does not require the use of expensive catalyst and allows for the use of readily available starting material to simplify separation procedures. The target compds. may be prepared according to the process of the invention as shown by the following example. Esterification of (3aR,7aS)-octahydroindole-2-carboxylic acid with benzyl alc. in the presence of p-toluenesulfonic acid in toluene followed by liberation of the free base with

triethylamine in dichloromethane, purification, and ester cleavage to give I. (S)-N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanine underwent intramol. heterocyclization with N,N'-carbonyldiimidazole to form N-carboxyanhydride III, which was amidated with I to give trandolapril (II).

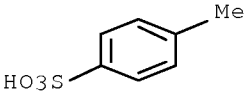
RX(1) OF 19 A + B + C ===> D...



A

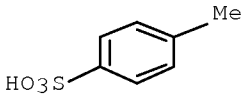


B

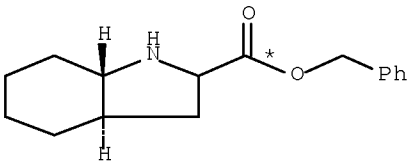


C

(1) →



D: CM 1



D: CM 2

RX(1) RCT A 881637-65-6, B 100-51-6, C 104-15-4
PRO D 881637-68-9
SOL 100-51-6 PhCH2OH
CON SUBSTAGE(1) reflux
SUBSTAGE(2) 3 hours, reflux

L2 ANSWER 7 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 147:522095 CASREACT Full-text
TITLE: Process for the preparation of trans-octahydro-1H-indole-2-carboxylic acid
INVENTOR(S): Debashish, Datta; Jagannath, Wani Mukesh
PATENT ASSIGNEE(S): Lupin Ltd., India
SOURCE: Indian Pat. Appl., 37pp.
CODEN: INXXBQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

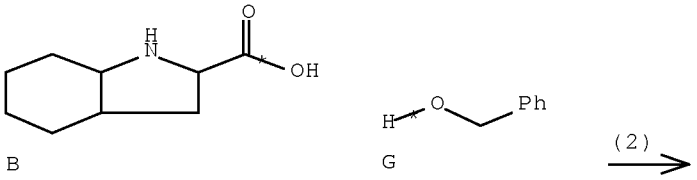
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 2003MU01033	A	20060120	IN 2003-MU1033	20031003

PRIORITY APPLN. INFO.: IN 2003-MU1033 20031003
GI

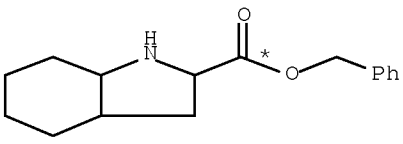
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a process for the preparation of octahydroindole-2-carboxylic acid of formula I, wherein the ring junction is trans, including enantiomers, esters, and salts thereof, and more specifically (2S, 3aR, 7aS)-octahydro-1H-indole-2-carboxylic acid (II) and esters and salts thereof. Compound II is a valuable intermediate in the synthesis of the angiotensin converting enzyme (ACE) inhibitor trandolapril. The process of the invention avoids the use of expensive, hazardous, toxic, and corrosive chems., very low temps., and gives about 50% of the trans-isomer, making the process of the invention more com. attractive than prior art. The target compds. may be prepared according to the process of the invention as shown by the following example. Rhodium-catalyzed hydrogenation of the hydrochloride of imino acid III in water under alkaline conditions gave about 1:1 mixture of the trans- and cis-isomers of I. Fractional crystallization of the mixture from methanol resulted in the isolation of II and its enantiomer. Acetylation followed by diastereomeric salt formation with cinchonidine and acidification gave IV with 99.7% optical purity. Compound IV underwent deacetylation with hydrochloric acid to give II, which may be used to prepare trandolapril (V) in a single step.

RX(2) OF 33 ...B + G ===> H



B G



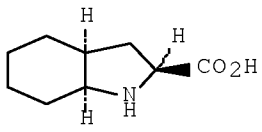
H

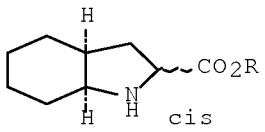
RX(2) RCT B 82717-40-6, G 100-51-6
RGT I 104-15-4 TsOH
PRO H 82717-90-6
SOL 110-82-7 Cyclohexane
CON 8 - 10 hours, 80 deg C

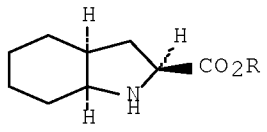
L2 ANSWER 8 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:206198 CASREACT Full-text
TITLE: Process for the preparation of intermediates of perindopril
INVENTOR(S): Joshi, Narendra Shriram; Ramam, Buddhavarapu Pattabhi; Bodkhe, Arjun Rajaram
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Limited, India
SOURCE: U.S. Pat. Appl. Publ., 7pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070032661	A1	20070208	US 2006-495102	20060728
IN 2005MU00903	A	20070706	IN 2005-MU903	20050803
PRIORITY APPLN. INFO.:			IN 2005-MU903	20050803
			US 2005-713000P	20050831

OTHER SOURCE(S): MARPAT 146:206198
GI


I

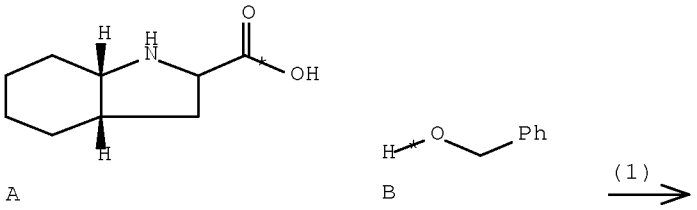

cis II


III

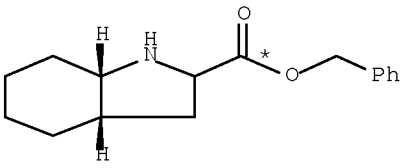
AB A process for the preparation of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid (I) is provided comprising (a) esterifying a cis-perhydroindole-2-carboxylic acid (II) with a first alc. of the formula ROH and a suitable free acid to provide the acid salt II.AS (Ad = acid), (b) reacting the acid salt with a first base to provide an ester (III), (c) treating the product of step (b) with an L-tartaric containing acid in a second alc. of the formula ROH to precipitate an ester salt III.L-tartarate, (d) reacting the ester salt with a second base to provide an ester III, and (e) hydrolyzing the ester to provide the desired compound I. Thus, cis-perhydroindole-2-carboxylic acid was esterified with benzyl alc. in the presence of p-toluenesulfonic acid under refluxing with azeotropic removal of water to give benzyl perhydroindole-2-carboxylate p-toluenesulfonate which was treated with triethylamine in CH2Cl2 to give benzyl cis-perhydroindole-2-carboxylate (IV). A solution of IV with methanol was treated with a solution of dibenzoyl-L-tartaric acid in methanol and the resulting mixture was stirred at 25° for .apprx.30 min, heated at .apprx.60° for .apprx.1 h, and cooled to 15°, followed by filtering the precipitated solid and drying at .apprx.60° to give benzyl (2S,3aS,7aS)-perhydroindole-2-carboxylate L-tartarate (V). V was added to CH2Cl2, treated

with aqueous NaOH solution, stirred for 1 h to give, after workup, benzyl (2S,3aS,7aS)-perhydroindole-2-carboxylate which was refluxed in a NaOH/aqueous methanol solution for .apprx.2 h, adjusted to pH .apprx.6 to .apprx.7 with dilute aqueous HCl solution, concentrated, treated with ethanol, refluxed, filtered to remove inorgs., and concentrated to give I. I was converted into perindopril tert-butylamine salt which is a prodrug for perindoprilat (angiotensin converting enzyme inhibitor) and used to treat hypertension.

RX(1) OF 24 A + B ===> C...



A B



C

RX(1) RCT A 923587-70-6, B 100-51-6

STAGE(1)
RGT D 104-15-4 TsOH
SOL 108-88-3 PhMe
CON SUBSTAGE(1) room temperature -> reflux
SUBSTAGE(2) 3 hours, reflux
SUBSTAGE(3) reflux -> 25 deg C

STAGE(2)
RGT E 121-44-8 Et3N
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(2) 30 minutes

PRO C 923587-72-8

L2 ANSWER 9 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:101038 CASREACT Full-text
TITLE: Process for industrially-viable preparation of perindopril erbumine
INVENTOR(S): Potluri, Ramesh Babu; Venkata Subramanian,

Hariharakrishnan; Mulakala, Atchuta Ramayya Chowdary;
Kodali, Hari Prasad
PATENT ASSIGNEE(S): India
SOURCE: PCT Int. Appl., 17pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006137082	A1	20061228	WO 2006-IN182	20060529

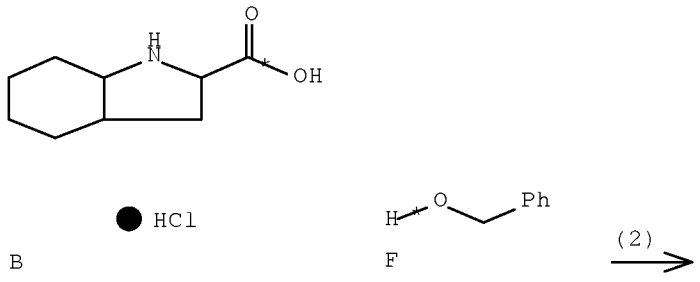
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

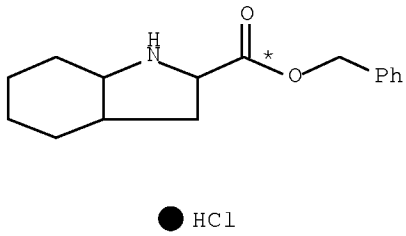
IN 2005CH00783	A	20070727	IN 2005-CH783	20050623

PRIORITY APPLN. INFO.: IN 2005-CH783 20050623
OTHER SOURCE(S): MARPAT 146:101038
AB A novel method for the preparation of perindopril erbumine [(2S,3aS,7aS)-1-[N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanyl]octahydro-1H- indole-2-carboxylic acid tert-butylamine salt] comprises treating (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid (I) esters with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanine, followed by deprotection and conversion to the erbumine salt. I benzyl ester hydrochloride was prepared from hexahydroindoline-2-carboxylic acid hydrochloride by catalytic hydrogenation, followed by esterification and resolution with dibenzoyl-L-tartaric acid or benzyloxycarbonyl-L-phenylalanine.

RX(2) OF 10 ...B + F ===> G...



B F



G

RX(2) RCT B 110623-68-2, F 100-51-6

STAGE(1)
RGT H 104-15-4 TsOH
SOL 108-88-3 PhMe
CON SUBSTAGE(2) 25 - 30 deg C

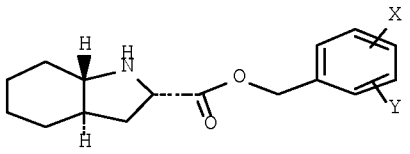
STAGE(2)
RGT I 7647-01-0 HCl
SOL 67-56-1 MeOH

PRO G 82717-97-3
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:7821 CASREACT Full-text
TITLE: Process for the preparation of (2S,3aR,7aS)-octahydroindole-2-carboxylates and their conversion to trandolapril
INVENTOR(S): Akhtar, Haider; Ramesh, Babu Potluri; Venkata, Subhramanian Hariharakrishnan; Hari, Prassad Kodali
PATENT ASSIGNEE(S): Sochinaz SA, Switz.
SOURCE: Eur. Pat. Appl., 19pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1724260	A1	20061122	EP 2005-76060	20050506
EP 1724260	B1	20080220		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
AT 386718	T	20080315	AT 2005-76060	20050506
PRIORITY APPLN. INFO.:			EP 2005-76060	20050506

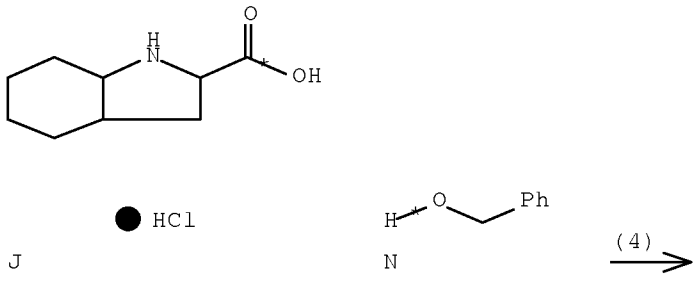
OTHER SOURCE(S): MARPAT 146:7821
GI



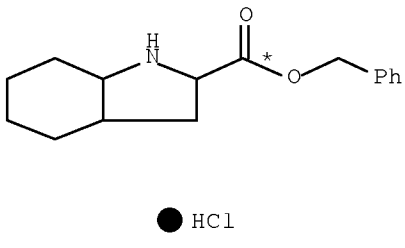
I

AB A process for preparation of benzyl (2S,3aR,7aS)-octahydroindole-2-carboxylate hydrohalide (I; X, Y = H, halo, alkyl, alkoxy), and its conversion to trandolapril comprises (a) reaction of Me β-hydroxyalaninate hydrochloride with an acylating agent in a nonpolar solvent to give a diacylated derivative, (b) reaction of the latter with a cyclohexanone enamine to give Me N-acyl-β-(2-oxocyclohexyl)alaninate, (c) hydrolytic cyclization to give an indole, (d) hydrogenation to a perhydroindole derivative, (e) esterification with a benzyl alc. followed by conversion of the benzyl ester arylsulfonate to the hydrohalide I, (f) resolution and conversion to a benzyl (2S,3aR,7aS)-octahydroindole-2-carboxylate hydrohalide, and (g) coupling with ECPPA (N-[(1-ethoxycarbonyl)-3-phenylpropyl]-(S)-alanine) acid chloride hydrochloride and debenzylating hydrogenolysis.

RX(4) OF 25 ...J + N ===> O...



J N



O

RX(4) RCT J 110623-68-2, N 100-51-6

STAGE(1)
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe
CON 3 hours, reflux

STAGE(2)
RGT P 1310-73-2 NaOH
SOL 7732-18-5 Water
CON pH 11

PRO O 82717-97-3

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

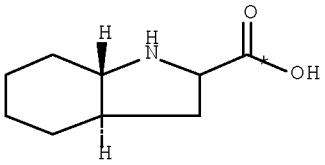
L2 ANSWER 11 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 144:350983 CASREACT Full-text
TITLE: Process for the preparation of (2S,3aR,7aS)-perhydroindole-2-carboxylic acid intermediate in synthesis of trandolapril
INVENTOR(S): Joshi, Narendra Shriram; Bhirud, Shekhar Bhaskar; Ramam, Buddhavarapu Pattabhi; Bodkhe, Arjun Rajaram
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Limited, India
SOURCE: U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060079698	A1	20060413	US 2005-245871	20051007
PRIORITY APPLN. INFO.:			US 2004-616934P	20041007
			US 2004-616959P	20041007

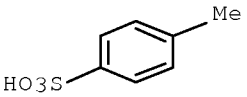
OTHER SOURCE(S): MARPAT 144:350983

AB Trandolapril intermediate (2S,3aR,7aS)-perhydroindole-2-carboxylic acid was prepared by a process which comprises esterification of (3aR,7aS)-perhydroindole-2-carboxylic acid with an alc. in the presence of an acid, reacting the acid addition salt with a base and then dibenzoyl-L-tartaric acid or di-p-toluoyl-L-tartaric acid and at least one alc., followed by addition of a second base and hydrolysis. (2S,3aR,7aS)-perhydroindole-2-carboxylic acid prepared by this method was used to prepare trandolapril.

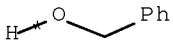
RX(1) OF 13 A + B + C ===> D...



A

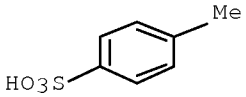


B

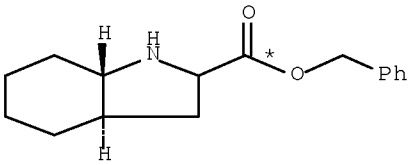


C

(1)



D: CM 1



D: CM 2

RX(1) RCT A 881637-65-6, B 104-15-4, C 100-51-6
PRO D 881637-68-9
SOL 108-88-3 PhMe
CON SUBSTAGE(1) reflux
SUBSTAGE(2) 3 hours, reflux

L2 ANSWER 12 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 144:171268 CASREACT Full-text
TITLE: Preparation of trandolapril
INVENTOR(S): Reddy, Pratap Padi; Chitre, Saurabh Shashikant; Polavarapu, Srinivas; Vakamudi Sri Naga Venkata Laxmi, Varaprasad
PATENT ASSIGNEE(S): Dr. Reddy's Laboratories Ltd., India; Dr. Reddy's Laboratories, Inc.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006014916	A2	20060209	WO 2005-US26423	20050726
WO 2006014916	A3	20060803		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,

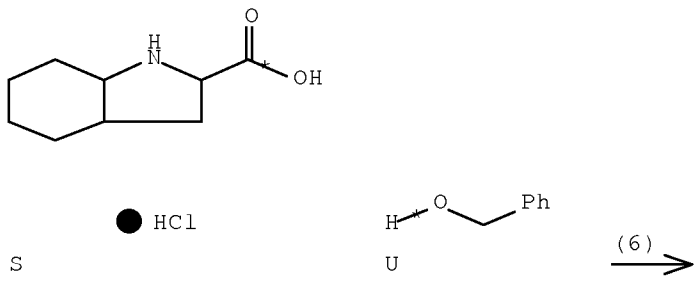
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

IN 2007CN00572 A 20070824 IN 2007-CN572 20070208

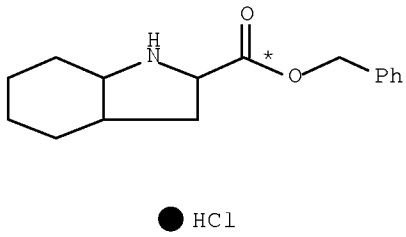
PRIORITY APPLN. INFO.: US 2004-591035P 20040726
US 2004-607839P 20040908
WO 2005-US26423 20050726

AB The invention relates to a process for preparing trandolapril, (2S,3aR,7aS)-1-[N-[(S)-1-carbethoxy-3-phenylpropyl]-L-alanyl]hexahydro-2- indolinecarboxylic acid, and intermediates formed in the process. Thus, (±)-benzyl octahydro-2-indolecarboxylate hydrochloride was treated with N-[(S)-1-carbethoxy-3-phenylpropyl]-L-alanine in CH2Cl2 in the presence of hydroxybenzotriazole and dicyclohexylcarbodiimide at 20-25°C for 3 h. Hydrogenation over 10% Pd on charcoal and workup, including recrystn., afforded trandolapril.

RX(6) OF 50 ...S + U ===> A...



S U



A

RX(6) RCT S 110623-68-2, U 100-51-6
RGT V 7719-09-7 SOCl2
PRO A 82717-97-3
SOL 100-51-6 PhCH2OH
CON SUBSTAGE(1) 2 - 3 hours, 0 - 10 deg C
SUBSTAGE(2) 14 - 16 hours, 25 - 35 deg C

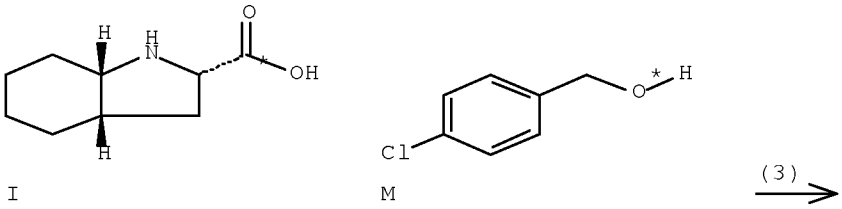
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:367597 CASREACT Full-text
TITLE: Process for the preparation of perindopril
INVENTOR(S): Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra
PATENT ASSIGNEE(S): Neopharma Limited, UK
SOURCE: Brit. UK Pat. Appl., 21 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

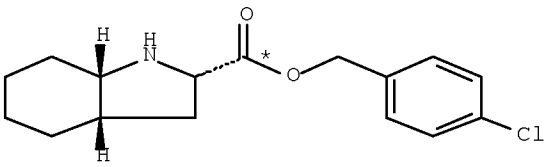
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2413128	A	20051019	GB 2004-8258	20040413
AU 2005232938	A1	20051027	AU 2005-232938	20050407
CA 2562843	A1	20051027	CA 2005-2562843	20050407
WO 2005100317	A1	20051027	WO 2005-GB1355	20050407
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1751107	A1	20070214	EP 2005-732439	20050407
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007532616	T	20071115	JP 2007-507836	20050407
IN 2006DN06462	A	20070831	IN 2006-DN6462	20061101
KR 2007054142	A	20070528	KR 2006-723684	20061113
US 20070185335	A1	20070809	US 2007-599918	20070409
PRIORITY APPLN. INFO.:			GB 2004-8258	20040413
			WO 2005-GB1355	20050407

OTHER SOURCE(S): MARPAT 143:367597

AB A process for preparing perindopril or a pharmaceutically-acceptable salt comprises coupling a 4-halo-, 4-alkoxy- or 4-nitrobenzyl ester of (2S,3aS,7aS)-2-carboxyoctahydroindole with N-[(S)-1-carbethoxybutyl]-L-alanine (1) in the presence of DCC and HOBT, followed by catalytic hydrolgenolysis. The starting ester was obtained from (S)-indoline-2-carboxylic acid by hydrogenation-esterification and 1 was obtained from norvaline Et ester and pyruvic acid under catalytic hydrogenation conditions. The method was applied to the synthesis perindopril erbumine (20.5 g obtained from 24 g 4-chlorobenzyl ester and 21.26 g 1).



I M (3)



N

RX(3) RCT I 80875-98-5, M 873-76-7
RGT O 104-15-4 TsOH
PRO N 793716-54-8
SOL 108-88-3 PhMe
CON reflux
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:44076 CASREACT Full-text
TITLE: A method for the preparation of (2S,3aR,7aS)-octahydro-1H-indole-2-carboxylic acid as key intermediate in the preparation of trandolapril by reacting a cyclohexyl aziridine with a dialkyl malonate
INVENTOR(S): Cid, Pau
PATENT ASSIGNEE(S): Texcontor Etablissement, Liechtenstein
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005054194	A1	20050616	WO 2004-EP13377	20041125

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1687271 A1 20060809 EP 2004-819621 20041125

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS

US 20070225505 A1 20070927 US 2007-580610 20070212

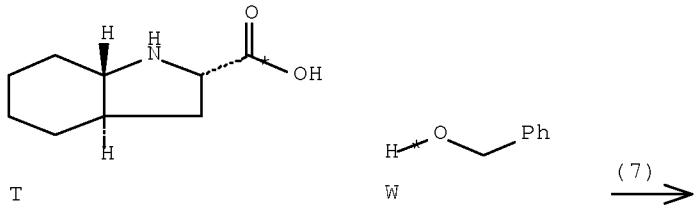
PRIORITY APPLN. INFO.: EP 2003-257417 20031125

WO 2004-EP13377 20041125

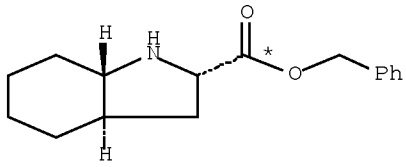
OTHER SOURCE(S): MARPAT 143:44076

AB Trandolapril intermediate (2S,3aR,7aS)-octahydro-1H-indole-2-carboxylic acid (or its C-protected derivs. or salts) was prepared by reacting a cyclohexyl aziridine with a dialkyl malonate to form a trans-fused 3-(alkylcarbonyl)octahydroindol-2-one, decarbonylation at the 3-position, conversion of 2-oxo group to an optionally protected carboxylic acid group, and removal of any N-substitution. Examples illustrate the synthetic method, starting with reaction of cyclohexene with chloramine-T to form N-tosylcyclohexanoaziridine.

RX(7) OF 36 ...T + W ===> X...



T W



X
YIELD 93%

RX(7) RCT T 87679-58-1, W 100-51-6
RGT Y 104-15-4 TsOH
PRO X 620973-54-8
SOL 108-88-3 PhMe

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 15 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 141:411226 CASREACT Full-text
TITLE: Process for preparation of perindopril and its salts
INVENTOR(S): Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra
PATENT ASSIGNEE(S): Cipla Limited, India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004099138	A2	20041118	WO 2004-GB2029	20040512
WO 2004099138	A3	20041223		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

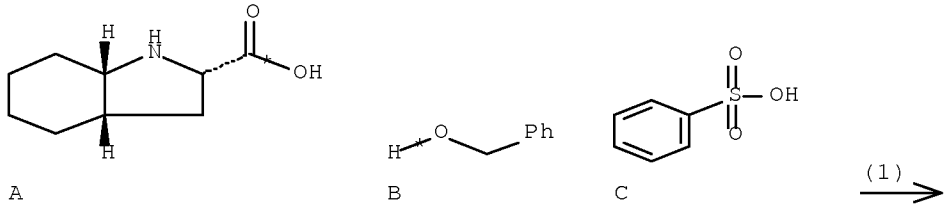
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IN 2003MU00468	A	20050211	IN 2003-MU468	20030512

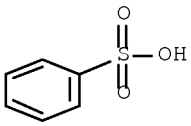
PRIORITY APPLN. INFO.: IN 2003-MU468 20030512
OTHER SOURCE(S): MARPAT 141:411226

AB A process for preparing perindopril or a pharmaceutically-acceptable salt comprises esterifying (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid (I) with benzyl alc. (or the 4-chloro or 4-alkoxy derivative) in the presence of benzenesulfonic acid as catalyst, treating the intermediate ester benzenesulfonate with N-[(S)-1-carbethoxybutyl]-L-alanine (II), and ester cleavage. Thus, I benzyl ester benzenesulfonate (40 g) was prepared, its suspension in CH2Cl2 made alkaline with aqueous ammonia, and the organic layer separated Treatment with II at 10-15 °C in the presence of hydroxybenzotriazole and N,N'-dicyclohexylcarbodiimide and workup afforded 43 g perindopril benzyl ester.

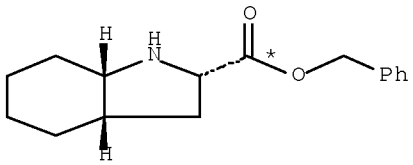
RX(1) OF 10 A + B + C ===> D...



A B C



D: CM 1



D: CM 2

RX(1) RCT A 80875-98-5, B 100-51-6, C 98-11-3
PRO D 793716-53-7
SOL 108-88-3 PhMe
CON 10 hours, reflux
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 16 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 141:140316 CASREACT Full-text
TITLE: Process for producing intermediate for trandolapril by esterification of racemic (2S,3aR,7aS)-hexahydroindoline-2-carboxylic acid with benzyl alcohol and optical resolution
INVENTOR(S): Shimamura, Hiroshi; Nakata, Yoshitaka
PATENT ASSIGNEE(S): Ohara Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004065368	A1	20040805	WO 2004-JP374	20040119

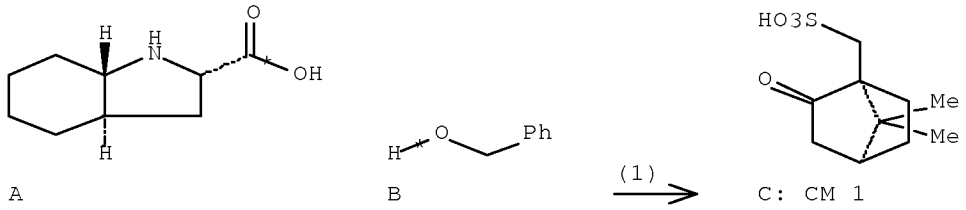
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ

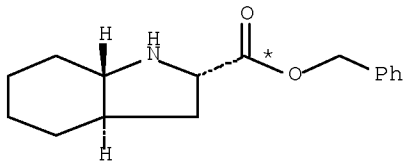
PRIORITY APPLN. INFO.: JP 2003-11889 20030121

AB Disclosed is a process for producing benzyl (2S,3aR,7aS)-hexahydroindoline-2-carboxylate (I), characterized by heating a racemic mixture consisting of (2S,3aR,7aS)-hexahydroindoline-2-carboxylic acid (II) and (2R,3aS,7aR)-hexahydroindoline-2-carboxylic acid (III), benzyl alc., and optically active 10-camphorsulfonic acid in a nonaq. solvent to convert the racemic mixture to benzyl esters, subjecting the diastereomeric salts of the benzyl esters with the optically active 10-camphorsulfonic acid which have been generated in the same reaction system to optical resolution based on a difference in solubility in an organic solvent, and then treating one of the isomers with a base. This process can simultaneously carry out esterification of a mixture of racemic II and III with benzyl alc. and optical resolution in one step in high yield, shortens the existing process by two steps, and is industrially advantageous. Thus, a racemic mixture of II and III 67.69, benzyl alc. 129.77, and (1R)-(-)-10-camphorsulfonic acid (IV) 97.57 g were added to toluene in a flask fitted with a condenser and a Dean-Stark separator, refluxed with stirring while

removing a theor. quantity of water, distilled under reduced pressure to remove the solvent (.apprx.650 mL), and treated with 800 mL tert-Bu Me ether at .apprx.60° with stirring. The precipitated crystals were collected by filtration, successively washed with toluene and tert-Bu Me ether , dried to give a crude crystalline diastereomer salt (189.5 g) which was recrystd. twice from toluene to give the diastereomer I.IV salt (63.5 g) which was added to a mixture of 315 mL tert-Bu Me ether and 63 mL H2O, treated dropwise with 130 mL 10.6% aqueous Na2CO3 solution, stirred for 10 min to give, after workup, 33.2 g I (64.0% from the racemate).

RX(1) OF 6 A + B ===> C...





C: CM 2

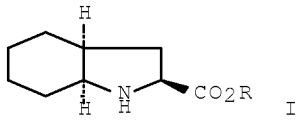
RX(1) RCT A 87679-58-1, B 100-51-6
RGT D 35963-20-3 l-Camphor-SO3H
PRO C 726698-12-0
SOL 108-88-3 PhMe
CON reflux
NTE benzyl esterification and optical resoln.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 17 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 139:69148 CASREACT Full-text
TITLE: Method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril
INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 11 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1323729	A1	20030702	EP 2003-290607	20030312
EP 1323729	B1	20041103		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 281465	T	20041115	AT 2003-290607	20030312
PT 1323729	T	20050228	PT 2003-290607	20030312
ES 2231760	T3	20050516	ES 2003-290607	20030312
WO 2004083237	A1	20040930	WO 2004-FR592	20040312
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

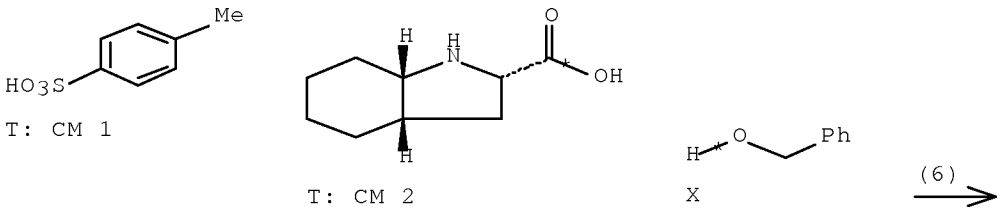
PRIORITY APPLN. INFO.: EP 2003-290607 20030312
OTHER SOURCE(S): MARPAT 139:69148
GI

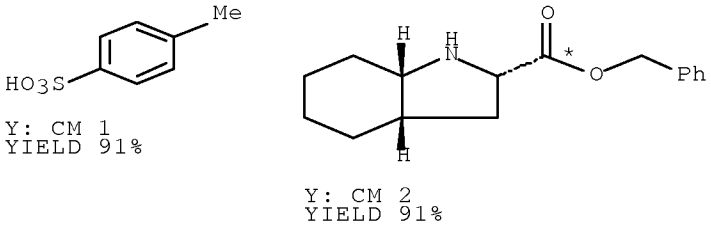


I

AB Title compds. I [R = H, CH2Ph, alkyl] were prepared by treating 2,7-oxepanedione with XCH2CH(NHR2)CO2R1 [R1 = CH2Ph, alkyl; R2 = protective group] to give HO2C(CH2)4COCH2CH(NH2)CO2R1 which was cyclized to the lactam, cyclized to the indole with Ti, and reduced over Pt, Pd, Rh, or Ni catalyst. Thus, I [R = H] was prepared from 2,7-oxepanedione and (2S)-ICH2CH(NHCO2CMe3)CO2CH2Ph in 5 steps.

RX(6) OF 27 ...T + X ===> Y





RX(6) RCT T 551940-10-4, X 100-51-6
PRO Y 94062-52-9
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

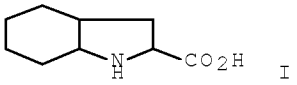
L2 ANSWER 18 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 111:77846 CASREACT Full-text
TITLE: Industrial preparation of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid as intermediate for antihypertensive perindopril
INVENTOR(S): Vincent, Michel; Baliarda, Jean; Marchand, Bernard; Remond, Georges
PATENT ASSIGNEE(S): ADIR, Fr.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 308339	A1	19890322	EP 1988-402337	19880916
EP 308339	B1	19920506		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2620703	A1	19890324	FR 1987-12900	19870917
FR 2620703	B1	19911004		
DK 8805149	A	19890318	DK 1988-5149	19880915
AU 8822361	A	19890323	AU 1988-22361	19880916
AU 618752	B2	19920109		
ZA 8806931	A	19890530	ZA 1988-6931	19880916

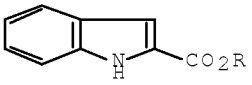
US 4935525	A	19900619	US 1988-245352	19880916
JP 02191251	A	19900727	JP 1988-232123	19880916
AT 75735	T	19920515	AT 1988-402337	19880916
ES 2033450	T3	19930316	ES 1988-402337	19880916
US 4954640	A	19900904	US 1990-462797	19900110
PRIORITY APPLN. INFO.:			FR 1987-12900	19870917
			EP 1988-402337	19880916
			US 1988-245352	19880916

OTHER SOURCE(S): MARPAT 111:77846

GI



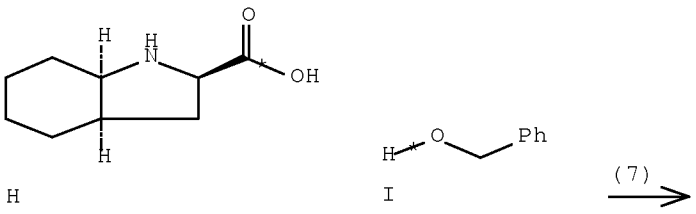
I



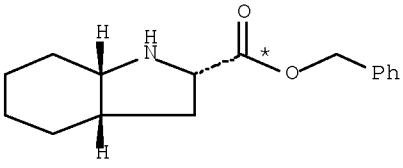
II

AB The title compound (I), useful as an intermediate for antihypertensive perindopril, was prepared from indolecarboxylic acid derivs. II (R = H, lower alkyl). Esterification of II (R = H) in EtOH containing H2SO4, reduction with Sn in EtOH containing HCl, saponification, and resolution gave (S)-indoline-2-carboxylic acid (III). Hydrogenation of III over Rh under H2 at 60° gave (2S,3aS,7aS)-octahydroindole-2-carboxylic acid.

RX(7) OF 27 ...H + I ===> J



H I



J

RX(7) RCT H 80828-13-3, I 100-51-6
PRO J 83508-14-9

L2 ANSWER 19 OF 22 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 109:231529 CASREACT Full-text

TITLE: Synthesis of S9490-3 [U-14C-cyclohexyl] 1-[(2S)2-[(1S)1-(ethoxycarbonylbutyl)amino]-1-oxopropyl]-(2S,3aS,7aS)-perhydroindole-2-carboxylic acid tert-butylamine salt and S9780 [U-14C-cyclohexyl] 1-[(2S)2-[(1S)1-(carboxybutyl)amino]-1-oxopropyl]-2S,3aS,7aS)-perhydroindole-2-carboxylic acid and of [3,4-3H-butylamino]S9490-3 and [(3,4-3H-)butylamino]S9780

AUTHOR(S): Pichat, L.; Tostain, J.; Gomis, J. M.; Coppo, M.; Moustier, A. M.; Vincent, M.; Remond, G.; Portevin, B.; Laubie, M.

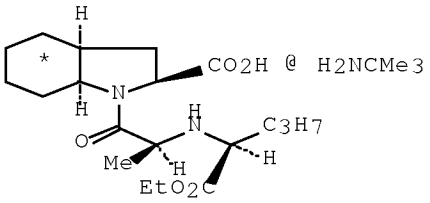
CORPORATE SOURCE: CEN Saclay, Gif sur Yvette, 91191, Fr.

SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1988), 25(5), 553-68
CODEN: JLCRD4; ISSN: 0362-4803

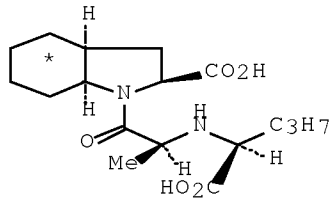
DOCUMENT TYPE: Journal

LANGUAGE: French

GI



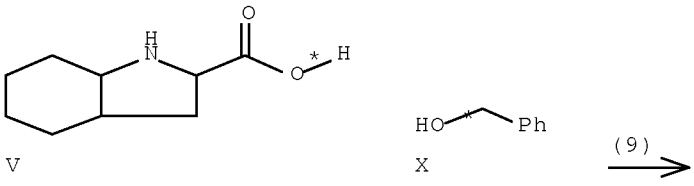
I



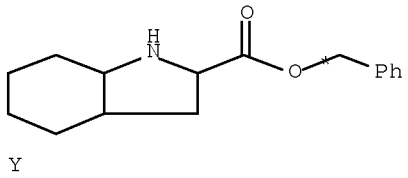
II

AB The title 14C-labeled compds. I (* signifies the uniform labeling of the cyclohexane ring with 14C) and II were prepared from aniline-U-14C in several steps. The title 3H-labeled compds. were also prepared The latter synthesis involved the tritiation of an allylglycine residue. The title compds. are potent inhibitors of angiotensin-converting enzyme.

RX(9) OF 69 ...V + X ===> Y...



V X



Y

RX(9) RCT V 117770-55-5, X 100-51-6
RGT Z 104-15-4 TsOH
PRO Y 117770-56-6
SOL 108-88-3 PhMe

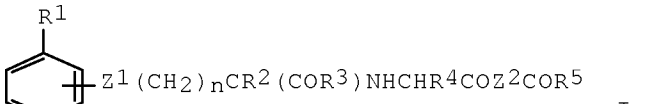
L2 ANSWER 20 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 105:79362 CASREACT Full-text
TITLE: Alanylindole antihypertensive agents
INVENTOR(S): Doll, Ronald J.; Neustadt, Bernard R.; Smith, Elizabeth M.; Magatti, Charles V.; Gold, Elijah H.
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 500,494, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4584285	A	19860422	US 1984-651378	19840917
WO 8701707	A1	19870326	WO 1985-US1744	19850916
W: AU, FI, HU, JP, KR, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8548088	A	19870407	AU 1985-48088	19850916
AU 581929	B2	19890309		
EP 236307	A1	19870916	EP 1985-904731	19850916
EP 236307	B1	19910417		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
HU 43620	A2	19871130	HU 1985-4245	19850916
HU 199507	B	19900228		
JP 63500938	T	19880407	JP 1985-504147	19850916
AT 62694	T	19910515	AT 1985-904731	19850916
IL 77451	A	19900712	IL 1985-77451	19851226
CA 1276396	C	19901113	CA 1986-499291	19860109
US 4691049	A	19870901	US 1986-831383	19860220
US 4783444	A	19881108	US 1986-849072	19860404
FI 8702110	A	19870513	FI 1987-2110	19870513
NO 8701982	A	19870513	NO 1987-1982	19870513
US 4840772	A	19890620	US 1988-227954	19880803

PRIORITY APPLN. INFO.:
US 1983-500494 19830602
US 1984-651378 19840917
EP 1985-904731 19850916
WO 1985-US1744 19850916
US 1986-849072 19860404

OTHER SOURCE(S): MARPAT 105:79362

GI



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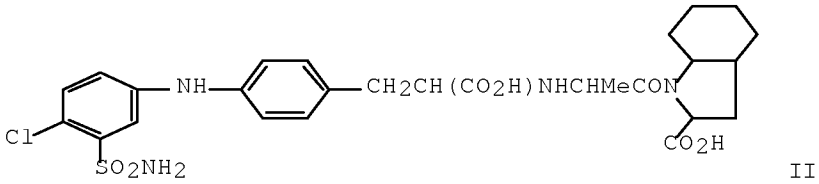
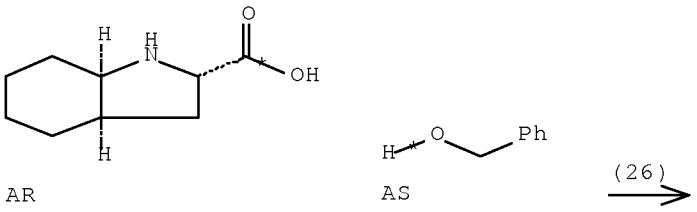


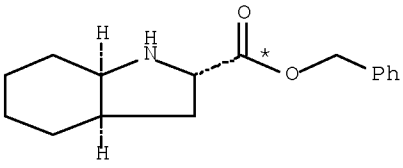
II

AB Amino acid derivs. I [R1 = benzothiadiazinylalkyl, chloro(sulfamoyl)benzamido, etc.; Z1 = CH2, CH2O, CH2S; n = 0-2; R2 = H, alkyl; R3, R5 = OH, alkoxy, etc.; R4 = H, alkyl, aminoalkyl; Z2 = proline residue, octahydroindole analog, etc.] were prepared, and they are useful as antihypertensives (no data). Alanine derivative II was prepared from the reaction product of 4-O2NC6H4CH2CH(NH2)CO2Et·HCl and BrCHMeCO2CMe3 in a series of reactions.

RX(26) OF 128 AR + AS ===> AT...



AR AS



AT

RX(26) RCT AR 87679-20-7, AS 100-51-6
PRO AT 124002-35-3
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 21 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 100:175294 CASREACT Full-text
TITLE: Carboxyalkyl dipeptides and pharmaceutical compositions containing them
INVENTOR(S): Smith, Elizabeth M.; Witkowski, Joseph T.; Doll, Ronald J.; Gold, Elijah H.; Neustadt, Bernard R.; Yehaskel, Albert S.
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: Eur. Pat. Appl., 134 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

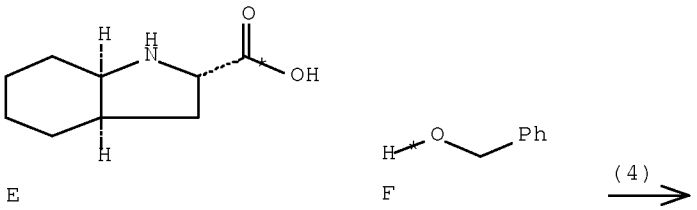
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 88350	A1	19830914	EP 1983-102014	19830302
EP 88350	B1	19850220		
R: AT, BE, CH, DE, FR, IT, LI, LU, NL, SE				
US 4431644	A	19840214	US 1982-355638	19820308
US 4431645	A	19840214	US 1982-355639	19820308
ZA 8300362	A	19840926	ZA 1983-362	19830119
AT 11921	T	19850315	AT 1983-102014	19830302
NO 8300737	A	19830909	NO 1983-737	19830303
AU 8312035	A	19830915	AU 1983-12035	19830303
AU 557795	B2	19870108		
GB 2117777	A	19831019	GB 1983-5837	19830303
GB 2117777	B	19850626		
DK 8301101	A	19830909	DK 1983-1101	19830304
JP 58162561	A	19830927	JP 1983-35707	19830304
FI 8300752	A	19830909	FI 1983-752	19830307
HU 29605	A2	19840228	HU 1983-781	19830307
HU 195520	B	19880530		
ZA 8301844	A	19840627	ZA 1983-1844	19830316

PRIORITY APPLN. INFO.:
US 1982-355638 19820308
US 1982-355639 19820308
US 1982-360532 19820322
ZA 1983-362 19830119
EP 1983-102014 19830302

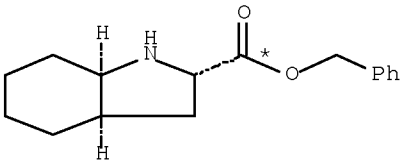
OTHER SOURCE(S): MARPAT 100:175294
GI For diagram(s), see printed CA Issue.
AB Title compds. RCH2CR1(CO2H)-NHCH[(CH2)nXR2]CO-X1-OH [R = alkyl, PhCH2, PhCH2O, PhCH2S, PhO, PhS; R1 = H, alkyl; X = S, R2 = substituted (3,4-dihydro-7-sulfamoyl-1,2,4-benzothiadiazin-3-yl 1,1-dioxide) methyl; X = NR3 (R3 = H, alkyl, Ph), R2 = sulfamoyl-substituted Bz, PhSO2, or benzyl; XR2 = sulfamoyl-substituted N-containing heterocyclic ring; n = 1-6; X1 = (un)substituted Pro or related N-containing heterocyclic amino acid residues] were prepared as antihypertensives and agents for the treatment of congestive heart failure and glaucoma (no data). Thus, H-L-Lys(Z)-OH (Z = CO2CH2Ph) was treated with PhCH2CH2COCO2Et and NaBH3CN to give (S)-PhCH2CH2CH(CO2Et)-L-Lys(Z)-OH, which was condensed with indole I to give dipeptide II (R4 = Z, R5 = CH2Ph), which was deblocked by hydrogenolysis to give II (R4 = R5 = H), which was

sulfonylated with 4-chloro-3-sulfamoylbenzenesulfonyl chloride to give title compound III.

RX(4) OF 16 ...E + F ===> G



E F



G

RX(4) RCT E 87679-20-7, F 100-51-6
PRO G 124002-35-3

L2 ANSWER 22 OF 22 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 100:139616 CASREACT Full-text
TITLE: Derivatives of bicyclic amino acids, agents containing them and their use, as well as bicyclic amino acids as intermediates
INVENTOR(S): Urbach, Hansjoerg; Henning, Rainer; Teetz, Volker; Geiger, Rolf; Becker, Reinhard; Gaul, Holger
PATENT ASSIGNEE(S): Hoechst A.-G. , Fed. Rep. Ger.
SOURCE: Eur. Pat. Appl., 103 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

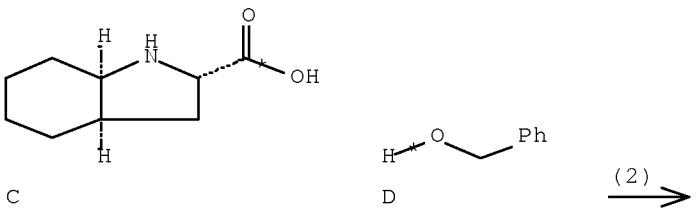
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 84164	A2	19830727	EP 1982-112007	19821224
EP 84164	A3	19831012		
EP 84164	B1	19870128		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
DE 3151690	A1	19830707	DE 1981-3151690	19811229
DE 3210701	A1	19831006	DE 1982-3210701	19820324

EP 170775 A1 19860212 EP 1985-103730 19821224
EP 170775 B1 19891108
EP 170775 B2 19941012
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE
AT 25244 T 19870215 AT 1982-112007 19821224
PRIORITY APPLN. INFO.: DE 1981-3151690 19811229
DE 1982-3210701 19820324
EP 1982-112007 19821224

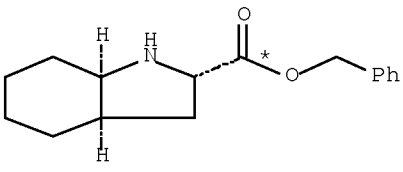
GI For diagram(s), see printed CA Issue.

AB Title compds. I [R = H, C1-6 alkyl, aminoalkyl, C2-6 alkenyl, C5-9 cycloalkyl, C5-9 cycloalkenyl, C5-7 cycloalkyl-C1-4 alkyl, (un)substituted aryl or partially hydrogenated aryl; R1 = H, C1-6 alkyl, C2-6 alkenyl, aryl-C1-4 alkyl; R2 = H, OH; R3 = H; R2R3 = O; R4 = C1-6 alkyl, C2-6 alkenyl, C5-9 cycloalkyl, (un)substituted aryl, indol-3-yl; n = 0, 1, 2] were prepared as antihypertensives due to their ability to inhibit angiotensin-converting enzyme (ACE). Thus, (S)-PhCH2CH2CH(CO2Et)-(S)-Ala-OH was condensed with (d,l)-2β,3aβ,7aβ-octahydroindole-3-carboxylic acid benzyl ester-HCl by DCC/1-hydroxybenzotriazole in DMF containing N-ethylmorpholine to give a mixture of the (2S,3aR,7aR)- and (2R,3aS,7aS)-diastereoisomers of octahydroindole II (R5 = Et, R6 = CH2Ph) (III). (2S,3AR,7aR)-III was debenzylated by hydrogenolysis and then saponified to give (2S,3aR,7aR)-II (R5 = R6 = H). (2S,3AR,7aS)-II (R5 = R6 = H) inhibited ACE in rats with an ED50 of 800 μg/kg.

RX(2) OF 6 C + D ===> E...



C D (2)



E

RX(2) RCT C 87679-20-7, D 100-51-6
PRO E 124002-35-3

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STN INTERNATIONAL LOGOFF AT 12:56:57 ON 08 MAR 2009